

CLAIMS

1. A method of introducing at least one organic molecule into one or more target cells comprising the passage of a supernatant, wherein the organic molecules are originally maintained, through a collection of target cells, which method comprises the steps of
- (a) providing isolated target cells in a reaction vessel, which target cells are capable of allowing entrance or actively taking up organic molecules; and
- (b) providing a supernatant comprising organic molecules;
- (c) contacting the organic molecules with the target cells by passing the supernatant through the reaction vessel so as to provide a fluidized or semi-fluidized bed of target cells in the reaction vessel,
- wherein the flow of supernatant through the reaction vessel is controlled to provide essentially constant conditions in the reaction vessel allowing a sufficient contact area and time to enable transfer of organic molecules from the supernatant into target cells.
2. A method according to claim 1, wherein the organic molecules are carriers of genetic information.
3. A method according to claim 1, wherein said organic molecules are nucleic acids, such as DNA or RNA.
4. A method according to claim 1, wherein the organic molecules prior to step (c) have been conjugated to a ligand and the target cells express a receptor for said ligand, such as the ligand lactose and hepatocytes expressing the asialoglycoprotein receptor as target cells.
5. A method according to claim 1, wherein the organic molecules are originally maintained within particles in the supernatant.
6. A method according to claim 5, wherein the particles are capable of interaction with the surface of a target cell.
7. A method according to claim 5, wherein said particles are virus, preferably retrovirus.
8. A method according to claim 5, which further comprises a step for the production of the particles, such as in a virus-producing cell line.

9. A method according to claim 1, which further comprises a step for separation of undesired material from the supernatant, such as cells producing organic molecules or particles comprising organic molecules.

10. A method according to claim 1, which further comprises a step wherein a sample of target cells is withdrawn and analysed as regards whether or not organic molecules have been introduced therein, and if required, the value of the flow rate through the vessel is reset to adapt the efficacy of transfer of organic molecules into target cells.

11. A method according to claim 1, wherein a direction of the supernatant is provided, which essentially counteracts the gravitational force of the target cells or alternatively essentially counteracts a force applied on the target cells, such as a centrifugal force.

12. A method according to claim 1, wherein the supernatant is passed more than one time through the target cells.

13. A recombinant cell, which has been genetically modified by introduction therein of an organic molecule in accordance with the method according to claim 1.

14. A cell according to claim 13, which has been genetically modified using a virus, such as a retrovirus, as the particle which originally comprised the organic molecule.

15. A system for the performing a method according to claim 1 which comprises -a reaction vessel (6) adapted to contain isolated target cells and -means for passing a supernatant comprising at least one organic molecule through a collection of isolated target cells,

characterised in that said means for passage of a supernatant through the target cells comprises tubing and a pumping means arranged to provide a fluidized or semi-fluidized bed of target cells and essentially constant conditions in the reaction vessel that allow transfer of organic molecules into target cells, said means for passage of a supernatant being arranged to provide a direction of flow, which essentially counteracts the gravitational force of the target cells or alternatively essentially counteracts a force applied on the target cells, such as a centrifugal force.

16. A system according to claim 15, wherein the reaction vessel is a column.

098744270.060601

17. A system according to claim 15, which further comprises means for recirculation of the supernatant through the target cells.

18. A system according to claim 15, which further comprises a supernatant vessel (4) for culture of particles producing or containing organic molecules.

5 19. A system according to claim 18, wherein a virus-producing cell line is cultured in the supernatant vessel (4).

20. A system according to claim 15, which further comprises means for the separation of undesired material.

09374270.050604